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Atty. Docket No.: 25436/2152

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Hogrefe, et al.
Serial No.: 10/035,091
Filed: December 21, 2001
Entitled: HIGH FIDELITY DNA
POLYMERASE
COMPOSITIONS AND USES
THEREOF

Examiner: R.G. Hutson
Group Art Unit: 1652
Conf. No.: 1719

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8a

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Kathleen M. Williams

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TRANSMITTAL LETTER

Enclosed for filing the above-identified patent application, please find the following documents:

1. Statement of Substance of Examiner Interview; and
2. Return Post Card.

The Commissioner for Patents is hereby authorized to charge any fees to Deposit Account No. 16-0085, Reference 25436/2152. A duplicate of this transmittal letter is enclosed for this purpose.

Respectfully submitted,

Date: July 28, 2004

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STATEMENT OF SUBSTANCE OF EXAMINER INTERVIEW

Sir:

Applicant hereby submits a written statement as to the substance of a telephone interview between Examiner Richard Hutson and Applicant's representatives, Barbara Gyure and Michelle Deng (hereinafter referred to as "Applicants") on June 21, 2004, in compliance with 37 C.F.R. § 1.133(b), and MPEP §§ 502.03 and 713.01. Applicants greatly appreciate Examiner Hutson for his clarification and discussion over rejections regarding pending claims 1-3, 6, 9-14, 18, 20-22 and 36-51, in particular, the lack of enablement and the obviousness rejections. Specifically, Examiner Hutson and Applicants agreed that the 112, first paragraph rejections over claims 3, 14, 44-47, 50 and 51, as well as the 103 rejections over claims 1-3, 10-14, 20, 22, 36, 37, 48 and 51, can be overcome as described below.

Rejections over Claims 3, 14, 44-47, 50 and 51 under 35 U.S.C. §112, First Paragraph for Lack of Enablement

Claims 3, 14, 44-47, 50 and 51 are rejected for lack of enablement because the Office Action states that biological material need to be deposited for the DNA polymerases recited in the claims. Examiner Hutson clarified during the interview that no deposit was required for any other DNA polymerases, but the claims were rejected for their recitation of "JDF-3 DNA polymerase." The Examiner felt that the JDF-3 DNA polymerase was not readily accessible to the public. Applicants argued that JDF-3 DNA polymerase was not only known in the art, but also readily accessible to the public as of the instant patent application filing date. For example, JDF-3 DNA polymerase was described on page 15 (line 15) of the specification as a DNA polymerase purified from *Thermococcus sp.*, with a Genbank accession number 2097756. The specification further pointed out that the JDF-3 DNA polymerase had a sequence of "sequence 12 from patent US 5602011." U.S. Patent 5,602,011 was issued February 11, 1997, four years before the filing date of the instant application. Applicant argued that it was routine technology to express and obtain a DNA polymerase with known sequence. No undue experimentation is required. Therefore, using the JDF-3 DNA sequence taught in the present specification, one skilled in the art would know how to make and use the invention as claimed in the present invention. As a result, no deposit was necessary to enable the invention as claimed, that is, to make and use an enzyme mixture comprising a first enzyme and a second enzyme, wherein the first enzyme is a JDF-3 DNA polymerase.

Examiner Hutson agreed with Applicants' above arguments, but maintained that the phrase "JDF-3 DNA polymerase," as used in the claims, even in view of the teachings in the specification, did not specifically disclose the particular JDF-3 sequence which would enable the make and use of the JDF-3 DNA polymerase in the claimed invention. Although Applicants disagreed with Examiner's reasoning, for the purpose of expediting the prosecution of the application, Applicants proposed to incorporate Sequence 12 of U.S. Patent No. 5602011 into the present specification so that it is clear to one skilled in the art as to what sequence the JDF-3 DNA polymerase would have. Applicants stated that such incorporation is allowed under MPEP 608.01(p), Examiner Hutson agreed that the incorporation of the particular sequence and its recitation in the claims would overcome the enablement rejections based on lack of biological deposits.

Rejections over Claims 1-3, 10-14, 20, 22, 36-37, 48 and 51 under 35 U.S.C. §103(a)

Examiner Hutson and Applicants also discussed the obviousness rejections over claims 1-3, 10-14, 20, 22, 36-37, 48 and 51 over Barnes et al. (U.S. Patent No. 5,436,149) and Komori et al. (2000).

Applicants argued that Barnes et al. only taught a formulation with a majority DNA polymerase component lacking 3'-5' exonuclease activity (e.g., Taq DNA polymerase) and a minority DNA polymerase component exhibiting 3'-5' exonuclease activity (e.g., wild type Pfu DNA polymerase). According to Barnes et al., such formulation was useful in increasing the efficiency and accuracy of PCR amplification of long DNA targets (column 16, lines 53-45). Barnes et al., the primary reference cited in the Office Action, did not teach a composition with two DNA polymerases, wherein both enzymes exhibiting 3'-5' exonuclease activities. Komori et al., the secondary reference cited, does not teach an enzyme mixture at all. Komori et al. simply teaches specific D405 Pfu mutants (i.e., D405A and D405E) that had reduced polymerase activity.

Applicants pointed out that the pending claims were drawn to an enzyme mixture comprising first and second enzymes. In all pending claims, the second enzyme was a mutant *Pfu* containing mutations reducing its polymerization activity. The second enzyme of the present invention as claimed, therefore, inherently exhibited 3'-5' exonuclease activity (exo^+) as known in the art. In some claims, e.g., claims 3, 14, 40-47, 49-50, the first enzyme was also an enzyme exhibiting 3'-5' exonuclease activity; while in other claims, e.g., claims 1-2, 10-13, 20, 22, 36-39, 48 and 51, the first enzyme was or might be an enzyme without 3'-5' exonuclease activity (exo^-).

With respect to claims drawn to an enzyme mixture containing two exo^+ enzymes such as claims 3, 14, 40-47, 49-50, Applicants argued that Barnes et al., the primary reference cited in the Office Action, did not teach a composition with two DNA polymerases, wherein both enzymes exhibiting 3'-5' exonuclease activities. Komori et al., the secondary reference cited, did not teach an enzyme mixture at all, therefore did not remedy the defect of Barnes et al.

Barnes et al. either alone, or in combination with Komori et al., therefore, did not teach the claimed subject matter of claims 3, 14, 40-47, 49-50. During the June 21, 2004 telephone interview, Examiner Hutson agreed that the references did not make Applicants' invention obvious when the claims are drawn to an enzyme mixture containing two enzymes, both of which have 3'-5' exonuclease activity, as in claims 3, 14, 40-47, 49-50.

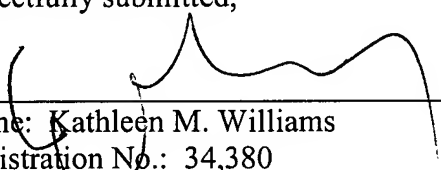
With respect to other claims, i.e., claims 1-2, 10-13, 20, 22, 36-39, 48 and 51, Applicants also believe that Barnes et al., either alone or in combination with Komori et al., does not make them obvious. However, for the purpose of expediting the prosecution and without acquiescing to the rejections, Applicants amended claims 1, 10, 12, 22, 36, and 48 so that they don't recite the amino acid position D405. During the telephone interview of June 21, 2004, Examiner Hutson agreed that such amendments would obviate the obviousness rejections.

We believed that no fees are due. However, if overlooked, the Commissioner for Patents is hereby authorized to charge all fees in the total amount to Deposit Account 16-0085, Reference No. 25436/2152.

Date:

July 28, 2004

Respectfully submitted,



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